

# Greater Nonesterified Fatty Acid Response in Men with Coronary Heart Disease\*

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THE notion that certain aspects of fat metabolism may play an important role in the genesis of coronary heart disease has been current for some years. Many observations of a relation to elevated serum cholesterol levels have been reported. Recently Albrink et al.<sup>1</sup> have indicated that the serum triglyceride concentration is significantly elevated in populations with early coronary heart disease, and that this measure, particularly in older age groups, has predictive value in estimating the risk of coronary occlusion. On the other hand, the plasma nonesterified fatty acids have not been widely studied in relation to this disease. This labile plasma fraction contains fatty acids that may be mobilized from body stores under the influence of epinephrine. Mobilization of fatty acids may, therefore, be expected to increase whenever epinephrine secretion increases. Rises in nonesterified fatty acid have been found to occur during fasting,<sup>2</sup> following cigarette smoking<sup>3</sup> and in association with fear, anger and anxiety.<sup>4</sup>

Piskorski<sup>5</sup> studied nonesterified fatty acid in men who had been hospitalized with acute coronary occlusions and found that their levels were comparable to those of a control group without coronary heart disease; however, his samples were drawn 10 to 29 days after the acute illness and obtained in the early morning under basal conditions of activity. Kershbaum et al.<sup>3</sup> recently reported that a group of men who had recovered from coronary occlusions had a greater nonesterified fatty acid response to cigarette smoking than did a group of controls. It is possible that men with proved coronary disease, under conditions of moderate activity and in the face of modest challenges such as those that are encountered during the course of daily life, might exhibit higher levels of nonesterified fatty

acid than controls. This possibility was investigated in a carefully designated group of 91 subjects, matched for age, occupation and social background, who were selected by random methods from the population of employees of a corporation with 22,295 men on the payroll.

## METHODS

To obtain subjects with coronary heart disease the medical records of all men 50 to 59 years old in one geographic division of the company who had been reported to have coronary occlusion were reviewed. From these were selected the records of all then actively employed men reported to have had an acute coronary occlusion one year or more previously, as manifested by typical signs, symptoms and course supported by electrocardiographic and laboratory evidence of infarction. Data were verified when necessary by information from hospitals and attending physicians. Twenty-three men who met the necessary criteria were thus identified and agreed to take part in the study when they were requested to do so.

Sixty-eight additional men from the same geographic division whose records and recent examinations showed no significant evidence of illness were then designated at random from the same population. These men were matched with the coronary subjects in age, occupation and educational backgrounds. These designated controls were examined clinically and were divided into two groups.

Thirty-three of the men in this group were found on examination to have one or more of the following abnormalities: a serum cholesterol concentration greater than 250 mg./100 cc., findings in the eye-grounds or peripheral vessels suggestive of atherosclerosis, blood pressure at examination or in the past greater than 140/90 mm. Hg, electrocardiographic changes suggestive of possible coronary heart disease, clinical obesity, or history of chest pain clinically suggestive of angina pectoris. Although none of these 33 men had clear-cut evidence of coronary heart disease, they were designated as a "high risk" group.

The remaining 35 men with none of the abnormali-

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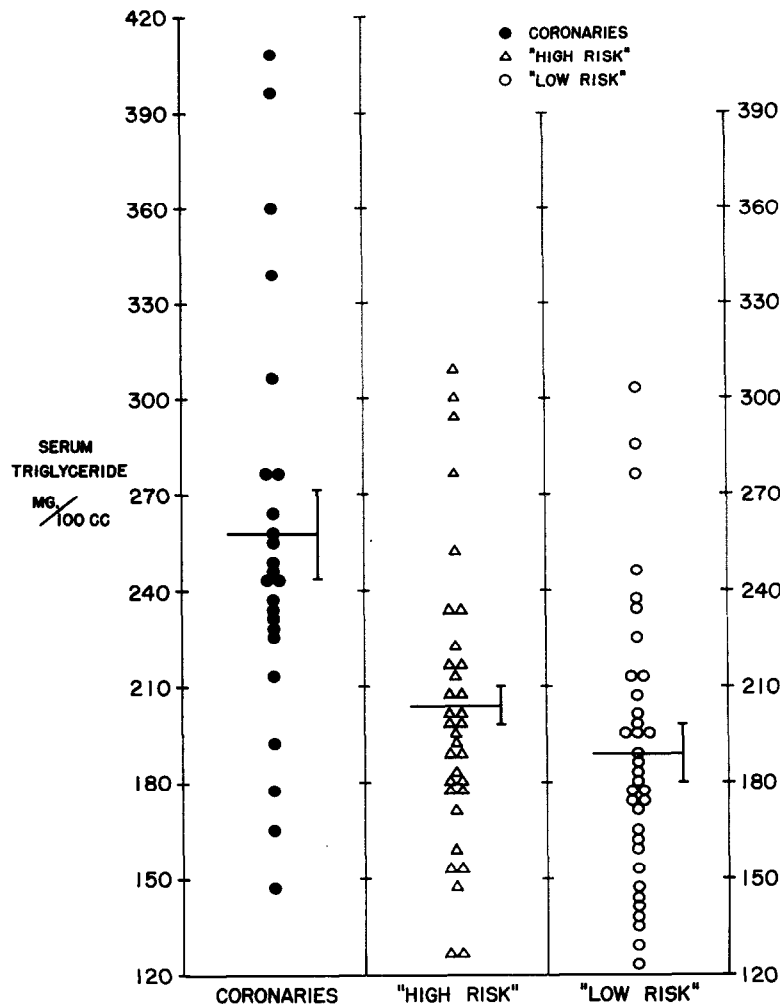


Fig. 1. Serum triglyceride levels in 91 men.

ties mentioned and no overt evidence of coronary heart disease were considered to have a statistically low risk of developing this syndrome and were designated as a "low risk group."

On the day of the study, the men arrived at the laboratory at approximately 9 A.M. They came singly on regular working days, having been excused from their usual duties by the company. Upon their arrival, blood was drawn for serum triglycerides and for plasma nonesterified fatty acid. The subjects spent the morning in a fasting state while a series of psychologic tests were administered to them. At noon, another blood sample for nonesterified fatty acid was obtained. Serum triglycerides were determined by the method of Hirsch.<sup>6</sup> Plasma nonesterified fatty acid was determined by the method of Dole.<sup>7</sup>

#### RESULTS

**Triglyceride Levels:** The men who had recovered from clinically typical coronary occlu-

sions had a significantly higher concentration of triglycerides in their serum than the men in the other two groups (Fig. 1). The mean value of 258 mg./100 cc. for the coronary subjects was different from the mean value of 189 mg./100 cc. for the "low risk" subjects with a probability of less than 0.001. It was different from the mean value for the "high risk" group of 204 mg./100 cc. within the same confidence limits. However, there was no significant difference between the values for the "low risk" and the "high risk" groups.

**Nonesterified Fatty Acid Levels:** The nonesterified fatty acid results are summarized in Figure 2. At 9 A.M. the coronary subjects had the highest mean value (836 mEq./L.) and the "low risk" subjects had the lowest mean value (734 mEq./L.), while the value for the "high risk" subjects lay between these two (751

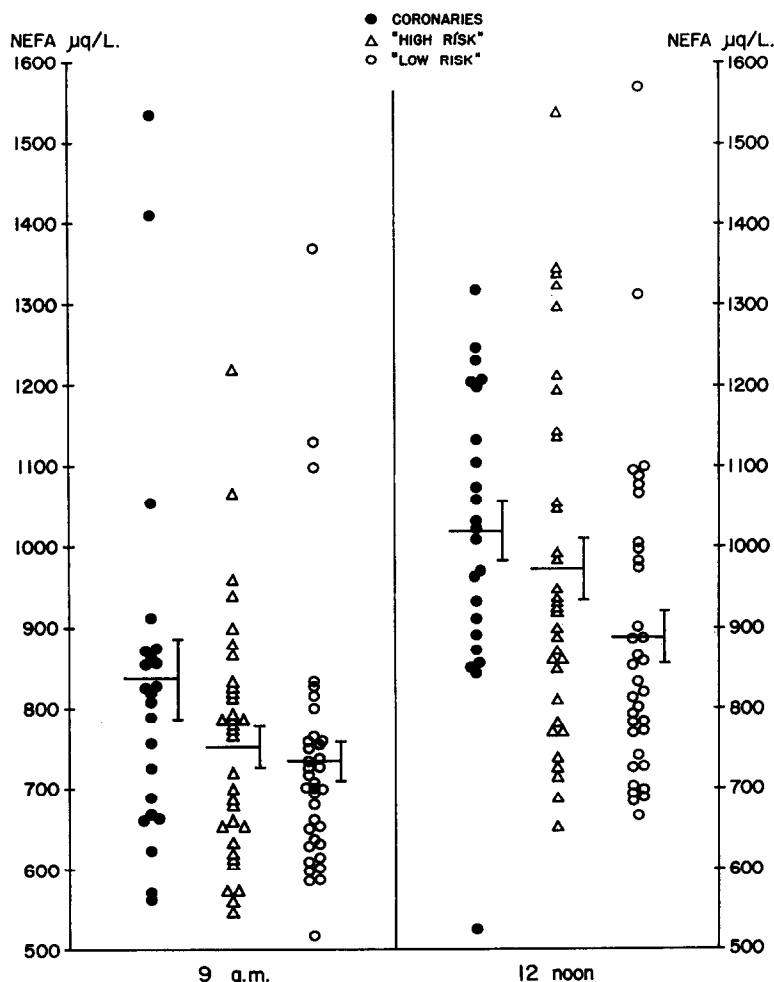


FIG. 2. Plasma nonesterified fatty acid levels in 91 men.

mEq./L.). At noon, values were in the same order. Coronary subjects had the highest value (1,019 mEq./L.), "low risk" subjects had the lowest (888 mEq./L.), and the "high risk" subjects were intermediate with a mean value of 972 mEq./L. The difference between the values for the coronary subjects and the "low risk" subjects at both 9 A.M. and at noon is significant at the 5 per cent confidence level, using the single-tail t test.

#### DISCUSSION

The differences in the values for serum triglycerides confirm other work which indicates that this fraction is often elevated in men who have coronary heart disease. Since this was a retrospective study, it is, of course, possible that the differences observed could have arisen from altered metabolism secondary to the previous

coronary occlusion. However, Albrink's data suggest that this measure has prospective value, so such an explanation appears to us unlikely.

The men who had recovered from coronary occlusions had initially higher concentrations of nonesterified fatty acid than did the men in the other two groups. During a morning of moderately challenging sedentary activity, the concentrations of nonesterified fatty acid rose to higher levels in all three groups. Both at 9 A.M. and at noon the values for the "high risk" group were intermediate between those of the coronary subjects and the "low risk" subjects. The intermediate position of the "high risk" subjects, who had evidence of coronary heart disease but no definite coronary occlusions, suggests that the high levels found in the "coronary" subjects were not simply a residuum of their acute illness. A quantitative difference in

the response of the subjects to the experimental situation might explain these differences in level of nonesterified fatty acid.

As attested by the subjects' statements and the psychologists' observations, the day of psychologic testing represented a moderate challenge to the subjects. Modest degrees of fear, anxiety or anger might have been aroused in many subjects, with consequent increases in nonesterified fatty acid. It is possible that the coronary subjects, who knew that they were being tested because they had had coronary occlusions, might find special significance in the day's events and be more fearful or anxious than the "low risks." This might explain their higher levels of nonesterified fatty acid. However, it is also possible that these men mobilized more fat in the face of a mild threat because they habitually react in such a manner during the ordinary course of their lives. Some recent studies have suggested that certain personality traits may be seen frequently in men who experience coronary occlusions.<sup>8,9</sup> They are said to be aggressive, hard-driving, somewhat hostile men who might be expected to react to a moderate challenge more vigorously than others. A further possibility is that the subjects with coronary artery disease have metabolically greater responses to the same amounts of epinephrine, mobilizing more fat than others in response to the same challenge.

#### SUMMARY

In a randomly designated sample of men carefully matched for age, occupation and social background, subjects who had recovered from

clinically typical coronary occlusions had higher concentrations of triglycerides in their serum than those who had not had such an illness. Their levels of nonesterified fatty acids were also initially higher and rose to higher levels in response to the moderately challenging sedentary tasks performed throughout a morning.

#### REFERENCES

1. ALBRINK, M. J., MEIGS, J. W. and MAN, E. B. Serum lipids, hypertension, coronary heart disease. *Am. J. Med.*, 31: 4, 1961.
2. BOGDONOFF, M. D., ESTES, H. E., JR., FRIEDBERG, S. J. and KLEIN, R. F. Fat mobilization in man. *Ann. Int. Med.*, 55: 328, 1961.
3. KERSHBAUM, A., BELLET, S., CAPLAN, R. F. and FEINBERG, L. J. Effects of cigarette smoking on free fatty acids in patients with healed myocardial infarction. *Am. J. Cardiol.*, 10: 204, 1962.
4. BOGDONOFF, M. D., ESTES, E. H., JR. and TROUT, D. Acute effect of psychological stimuli upon plasma non-esterified fatty acid level. *Proc. Soc. Exper. Biol. & Med.*, 100: 503, 1959.
5. PISKORSKI, J. M. and Man, E. B. Serum non-esterified fatty acid in patients with recent myocardial infarctions. *Proc. Soc. Exper. Biol. & Med.*, 100: 473, 1959.
6. HIRSCH, J. and AHRENS, E. H., JR. The separation of complex lipid mixture by the use of silicic acid chromatography. *J. Biol. Chem.*, 233: 311, 1958.
7. DOLE, V. P. A relation between non-esterified fatty acids in plasma and the metabolism of glucose. *J. Clin. Invest.*, 35: 150, 1956.
8. FRIEDMAN, M. and ROSENMAN, R. H. Association of specific overt behavior pattern with blood and cardiovascular findings. *J.A.M.A.*, 169: 1286, 1959.
9. OSTFELD, A. M., LEBOVITS, B. Z., SHEKELLE, R. B. and PAUL, O. A prospective study of the relationship between personality and coronary heart disease. Unpublished data.